



RotaShield® (Rotavirus) Vaccine and Intussusception

What is RotaShield® vaccine?

RotaShield® (rotavirus) vaccine was the first effective vaccine to prevent rotavirus gastroenteritis approved for use in the United States. Rotavirus is the most common cause of severe diarrhea among children, resulting in the hospitalization of approximately 55,000 children each year in the United States and the death of more than 600,000 children annually worldwide.

What is intussusception?

Intussusception is an uncommon type of bowel obstruction that occurs when the bowel folds in on itself. Intussusception is most common among young children. Some cases occur with viral infection, or when a piece of enlarged tissue serves as a "lead point" (e.g., polyp or enlarged lymph gland), but no cause is identified in most cases. The most common place in the intestine for intussusception to occur is where the small bowel joins the large bowel. However, intussusception can occur in many parts of the intestine. With prompt treatment, almost all patients fully recover.

Did RotaShield® vaccine cause intussusception?

In the United States, some infants developed an uncommon but potentially life threatening form of intestinal obstruction called intussusception soon after RotaShield® began to be used in October 1998. At first, it was not clear if the vaccine or some other factor was causing the intussusceptions. The CDC quickly recommended that use of the vaccine be suspended until this question could be answered, and immediately started two emergency investigations to find out if receiving RotaShield® vaccine was causing some of the cases of intussusception.

The results of the investigations showed that RotaShield® vaccine caused intussusception in some healthy infants less than 12 months of age who normally are at low risk for this condition. The risk of intussusception increased 20 to 30 times over the expected risk for children of this age group within 2 weeks following the first dose of RotaShield® vaccine. The risk increased 3 to 7 times over the expected risk for this age group within 2 weeks after the second dose of RotaShield® vaccine. There was no increase in the risk of intussusception following the third dose of RotaShield® vaccine, or when three weeks had passed following any dose of the vaccine.

Intussusception from all other causes is most common among infants in the first year of life; 1 in 2,000 to 1 in 3,000 infants is affected before one year of age. Based on the results of the investigations, CDC estimated that 1 or 2 extra cases of intussusception would be caused among each 10,000 infants vaccinated with RotaShield® vaccine.

Was intussusception suspected before RotaShield® vaccine was licensed?

Among participants of 27 pre-licensing trials of several candidate rotavirus vaccines, five cases of intussusception occurred among 10,054 (0.05%) vaccinees; all were among infants

who received a second or a third dose of vaccine. One case of intussusception occurred among 4,633 (0.02%) infants who received a placebo vaccine. The difference was not statistically significant between the groups. Careful evaluation was undertaken to evaluate if a relationship between receipt of the RotaShield® vaccine and intussusception might have occurred. None was found. As a precaution, intussusception was listed in the package insert of the vaccine as a possible adverse reaction, and physicians were encouraged to report adverse reactions of all kinds to the Vaccine Adverse Event Reporting System.

How many infants received RotaShield® vaccine before it was withdrawn from use?

In studies before RotaShield® vaccine was licensed, about 7,000 infants received the vaccine. After RotaShield® vaccine was licensed, many more infants were vaccinated during 9 months that the vaccine was available. However, the exact number of infants who received RotaShield® is not known. In the two investigations conducted by CDC, overall, fewer than 13% of infants who were less than one year of age had been vaccinated with one or more dose of the three dose series.

Is the vaccine still available in the US?

RotaShield® vaccine is no longer available for use in the United States.

What action did CDC take when cases of intussusception were reported to VAERS?

CDC, in collaboration with the FDA, and state and local health departments throughout the US conducted two large investigations. One was a multi-state investigation which evaluated whether or not rotavirus vaccine was associated with intussusception. Based on the results of the investigation, CDC estimated that RotaShield® vaccine increased the risk for intussusception by 1 or 2 cases of intussusception among each 10,000 infants vaccinated. The other was a similar investigation in children vaccinated at large managed care organizations. When the results of these investigations were became available, the Advisory Committee on Immunization Practices (ACIP) withdrew its recommendation to vaccinate infants with RotaShield® vaccine, and the manufacturer voluntarily withdrew RotaShield® from the market in October 1999.

Why did the Advisory Committee on Immunization Practices take this action?

A primary goal of the CDC is to protect the health and safety of the general public in the United States. One of the most effective ways to prevent disease is through vaccination. However, when a vaccine is discovered to have a serious side effect, a recommendation to continue using the vaccine will be reconsidered and the vaccine may be withdrawn, in spite of the beneficial effect of the vaccine to prevent disease. The decision to stop recommending use RotaShield® vaccine in the United States was made by the ACIP, American Academy of Pediatrics (AAP) and the American Academy of Family Physicians (AAFP), because intussusception is a serious condition and because of the perception that most of the severe complications of rotavirus gastroenteritis in the United States can be prevented by oral rehydration. The vaccine safety monitoring systems we currently have in place worked to detect an uncommon side effect and to assure the safety of infants who receive routine vaccinations. Vaccination was promptly suspended and new cases of intussusception were prevented.

Are there other vaccines to prevent rotavirus gastroenteritis?

Currently, no rotavirus vaccine is available in the United States, except as part of research on new vaccines. Promising vaccines are being tested but they have not been licensed for use in the US. Until a new rotavirus vaccine becomes available, oral fluid hydration and prompt medical evaluation remain the most effective means to prevent serious complications of rotavirus gastroenteritis, as well as severe diarrhea due to other causes in young children.

If a child develops intussusception or any serious reaction after a vaccine, whether or not it is thought to be related to the vaccine, the child should receive prompt medical attention and the reaction should be reported to the Vaccine Adverse Event Reporting System (VAERS). VAERS reporting forms and information can be requested 24 hours a day by calling (800) 822-7967 or by via the World Wide Web at: <http://www.vaers.org>

Suggested Reading:

Intussusception among recipients of rotavirus vaccine—United States, 1998-1999. MMWR Morb Mortality Wkly Rep 1999;102:1483-91.

Glass RI, Kilgore PE, Holman RC, et al. The epidemiology of rotavirus diarrhea in the United States: surveillance and estimates of disease burden. J Infect Dis 1996;174:Suppl 1:S5-S11.

Kramarz P, France EK, DeStepfano F, et al. Population-based study of rotavirus vaccination and intussusception. Pediatr Infect Dis J (in press)

Murphy TV, Gargiullo PM, Massoudi MS, et al. Intussusception among infants given an oral rotavirus vaccine. N Engl J Med 2001;344:564-72.

Rennels MB. The rotavirus vaccine story: a clinical investigator's view. Pediatrics 2000;106:123-5.

Zanardi L, Haber P, Mootrey GT, et al. Intussusception among recipients of rotavirus vaccine: reports to the Vaccine Adverse Event Reporting system. Pediatrics